REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated January 13, 2004. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 3, 5-7, 14-15, and 23 are under consideration in this application. Claims 1-2, 4, 8-13 and 16-22 are being cancelled without prejudice or disclaimer. Claims 3, 5-7, and 14-15 are being amended, as set forth above, in order to more particularly define and distinctly claim Applicants' invention. A new claim 23 is being added to recite other embodiments described in the specification.

Additional Amendments

The claims are being amended to correct formal errors and/or to better disclose or describe the features of the present invention as claimed. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Formality Rejection

Claim 22 was rejected 35 U.S.C. § 101 due to the claiming of non-statutory subject matter, namely a computer program not embodied in a computer-readable media. As claim 22 is being cancelled without prejudice or disclaimer, the objection thus becomes moot. Claims 1-22 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. As indicated, the claims have been cancelled or amended as suggested or required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejections is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claims 1-9 and 16-22 were rejected under 35 U.S.C. § 102(b) as being anticipated by the article of Hartenstein et al., *Trends in Genetics,* 1995 ("Hartenstein"), and claim 3 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Hartenstein in view of U.S. App. 2003/0176977 A to Allen *et al.* ("Allen"). In addition, claims 10-13 were rejected as being unpatentable over Hartenstein in view of the article to Martinelli *et al.*, *Cell & Development Biology*, 1997 ("Martinelli"), and claims 14-15 were rejected as being unpatentable over Hartenstein in view of the article to Debry *et al.*, *Genomics*, 1996 ("Debryl"). Lastly, the prior art article of Baldock *et al.*, "3-D Reconstructions for Graphical Databases of Gene Expression, *Cell & Development Biology*, 1997, vol. 8, pp. 499-507) were cited as being pertinent to the present application. These rejections have been carefully considered, but are most respectfully traversed.

The method for displaying a gene expression phenomenon in one or more living organisms (e.g., p. 3, line 3: human; p. 13, last line: Ascidian/sea squirt[1]) in a system comprising memorizing means that memorizes, for each cell or each site (e.g., "*a lung or a liver*" p. 16, line 22) of said living organisms along a time axis, data indicative of a shape of said cell or site and expression data associated with a degree of expression of the gene expression phenomenon in said cell or site along a time axis; and processing means adapted to obtain said data indicative of the shape and expression data that are memorized in said memorizing means to visualize and display the gene expression phenomenon on a display screen, as now recited in claims 3, 5-7 and 14-15, comprising: a first step of displaying as a three-dimensional image on the display screen a shape of said living organisms of which the gene expression phenomenon is observed; a second step of setting a viewpoint on a three-dimensional space where the gene expression phenomenon in said living organisms displayed is to be observed; and a third step of reading the gene expression data of said cell or site of said living organisms out of said memorizing means, creating a plurality of three-dimensional images representing the gene expression phenomenon at the viewpoint set at said second step or at a fixed viewpoint, to display at least one of said three-dimensional images in multiple tones

[1] AHox1 is an Ascidian (*Halocynthia roretzi/* sea squirt) homeobox gene; AMD1 is an Ascidian gene developed into body wall muscle in adult stage; and As-T is an ascidian homologue (As-T) of the mouse T gene.

using one color or multiple colors, each of the tones corresponding to a degree of expression of the gene expression phenomenon.

In particular, the invention (**claim 3**) chronologically displays a change in shape of said cell or site of said living organisms caused by an external stimulation (p. 37, lines 7-8; Fig. 37) and a change in shape of a cell or site caused by internal activities; and displaying an animation of a three-dimensional image representing the gene expression phenomenon from a certain viewpoint at a certain instant of time.

As such, the invention can three-dimensionally display not only embryogenesis, i.e., an inherent biological phenomenon, but also changes in response to external stimulation. The external stimulation may be thermal change, environment composition change, addition of inorganic or organic chemical materials from outside, electrical stimulation, and the like. The gene expression data is stored in a database indicated in the present invention as "experimentally observed data (p. 1, last paragraph)" concerning one or more living organisms so as to display the ***actual*** result of planned experiments on a life form, rather than just ***natural*** phenomena or simulations.

The three-dimensional visualization of explicit factors and biological reactions enables an unprecedentedly effective method for revealing a network system of gene expressions which is a key for clarifying basic biological phenomena in physiology, pathological causes, side effects of medication, or the like. In other words, by three-dimensionally observing the actual change in gene expression in response to external stimuli, it becomes possible to not only reveal a gene network of related genes, but also discover an alternate route of gene expression, for example, by altering the parameters. The invention thus displays very important information for genomic analysis.

In contrast, Hartenstein merely displays *natural* phenomena, i.e., embryogenesis, and Allen merely displays simulated cellular biochemical pathways (Title; "*to access the influence of a given stimulus on a biochemical pathway*" (Abstract; [0115][0123]; Figs. 11 & 15) caused by some external stimulus (e.g., pharmaceutical compounds or toxic substances [0009]) so as "*to predict likely biological outcomes* ([0013])," rather than just faithfully displays the outcomes or gene expression as the invention.

One skilled in the art will not be motivated to combine the teachings in Hartenstein and Allen in the manner suggested by the Examiner since the resulting change in the principle of operation in Hartenstein, i.e., displaying actual embryogesis images, will contradict its intended purpose. It is well established that a rejection based

on a principle, simulation in Allen, that contracts the teachings of the primary reference Hartenstein is improper.

Even if, arguendo, a person of ordinary skill were motivated to combine the teachings in Hartenstein and Allen, such combined teachings would still fall short in fully meeting the Applicants' claimed invention as set forth in claim 3 since, as discussed, there is no teaching of "three-dimensionally display ***actual*** changes in gene expression in response to ***external*** stimulation" in either Hartenstein or Allen.

The invention **(claim 5)** displays in parallel three-dimensional images representing expression phenomena for each cell or site of said living organisms of **multiple species** (2901, 2902 in Fig. 29; 3001 and 3002 in Fig. 30; "*the cells of two living matters*" p. 35, 1st paragraph; p.3, line 3; p. 32, 2nd paragraph); comparing the three-dimensional images representing the gene expression phenomena for each cell or site of said living organisms of multiple species to visually display similarities therebetween in a predetermined display format.

The invention displays of not only the embryogenesis of a single type of living organism, but also a comparative display of the gene expressions of a plurality of living organisms three dimensionally so as to analyze what adaptations occur among gene networks in the process of evolution, and a difference in a gene network of gene groups which is responsible for the difference that leads to a species-specific branching. Also, as compared with a method for visualizing the embryogenesis of a **single species**, the invention makes it possible to clarify a specialized role of a gene function in ontogenesis in higher dimensions by comparing the information being expressed in each site/organ. Visualizing three-dimensional differences among **multiple species** makes it possible to prove relationships between evolution and expression, so that functions of individual genes and their relations can be speedily discovered without conducting some experiments that are expensive or involve ethical problems.

In contrast, Hartenstein merely display the same embryo (of one **single species**) at two different stages.

The invention **(claim 6)** maps expression data of a cell or site along a time axis to be displayed in one color or multiple colors in various scales depending on a gene expression frequency in said cell or site. The invention **(claim 7)** also maps expression data of two or more cells or sites on coordination points along an axis to display in one

color or multiple colors in various scales a change in gene expression frequency in said cells or sites in parallel. See Fig. 26; p. 34, 1st full paragraph.

The invention effectively displays the expression of a specified gene in a three-dimensional manner using three primary colors. This enables a dynamic display of the relationships among multiple genes, which was impossible by merely displaying a change in a single gene in terms of embryogenesis in chronological order. Thus, the sequence of events wherein an increase of expression of a certain gene brings about an increase or decrease of expression of another gene, which affects other factors, and so on, can be visualized. This effective method also supports the effects of claims 3 and 5.

The invention (**claim 14**) coordinates and displays, in a predetermined display format, a three-dimensional image of the expression phenomenon and a position of a gene on a gene map that causes the gene expression phenomenon. The invention (claim 15) coordinates and displays, in a predetermined display format, three-dimensional images of the expression phenomenon of a gene in two or more cells or sites and a position of the gene on a gene map that causes the expression phenomenon.

The present relates information about visualized networks among genes that are expressed with locations on the chromosome from which the genes are derived, thereby making it possible to discover information that can contribute to the clarification of expression controlling mechanisms. The method enables visualizing how information about the frequency of actual expression varies on the chromosomes from which the genes are derived. Also, the method visualizes the relationship of genetic sequences on a map simultaneously with the relationship of gene networks so as to relate or predict three-dimensional expression information based upon the known information on a chromosome map, and further to efficiently narrow the candidate gene sequences to be visualized and clarified.

As admitted by the Examiner, Hartenstein fails to teach "*coordinating the tree-dimensional image of gene expression phenomenon with the position of a gene responsible for the gene expressio*n (p. 15, 4th paragraph of the outstanding office action)." Debry was relied upon by the Examiner to cover such a feature. However, as admitted by the Examiner; Derby fails to teach "*displaying a three-dimensional image of a gene expression phenomenon in a cell , tissue or organism* (p. 15, 4th paragraph)."

Although the invention displays the general gene map as in Debry, the invention display the gene map along with "*a three-dimensional image of a gene expression phenomenon in a cell or site of a living organism*" to achieve unexpected results or properties. For example, to discover information that can contribute to the clarification of expression controlling mechanisms. The presence of these unexpected properties is evidence of nonobviousness. MPEP§716.02(a).

> "*Presence of a property not possessed by the prior art is evidence of nonobviousness. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (rejection of claims to compound structurally similar to the prior art compound was reversed because claimed compound unexpectedly possessed anti-inflammatory properties not possessed by the prior art compound); Ex parte Thumm, 132 USPQ 66 (Bd. App. 1961) (Appellant showed that the claimed range of ethylene diamine was effective for the purpose of producing " 'regenerated cellulose consisting substantially entirely of skin' " whereas the prior art warned "this compound has 'practically no effect.' ").*

Applicants will point out that "[t]*he submission of evidence that a new product possesses unexpected properties does not necessarily require a conclusion that the claimed invention is nonobvious. In re Payne, 606 F.2d 303, 203 USPQ 245 (CCPA 1979). See the discussion of latent properties and additional advantages in MPEP § 2145*." However, the three unexpected properties were unknown and non-inherent functions in view of Debry, since Debry does not inherently achieve the same results. In other words, these advantages would not flow naturally from following the teachings of Debry, since Debry fails to suggest "displaying the gene map along with a three-dimensional image of a gene expression phenomenon in a cell or site of a living organism".

Applicants further contend that the mere fact that one of skill in the art could rearrange Hartenstein and Debry to meet the terms of the claims is not by itself sufficient to support a finding of obviousness. The prior art must provide a motivation or reason for one skilled in the art to provide the unexpected properties, such as "displaying the gene map along with a three-dimensional image of a gene expression phenomenon in a cell or site of a living organism", without the benefit of appellant's specification, to make the

necessary changes in the reference device. *Ex parte Chicago Rawhide Mfg. Co.*, 223 USPQ 351, 353 (Bd. Pat. App. & Inter. 1984). MPEP§2144.04 VI C.

The invention (**claim 23**) maps expression data of a cell or a site of a plurality of genes of one living organism on coordination points on a cylindrical plane (e.g., 106 in Fig. 1, 3402 in Fig. 34), said expression data of each of the plurality of genes being shown as a bar with a height corresponding to a degree of one respect gene expression phenomenon.

The invention effectively displays the expression of a specified gene in a three-dimensional manner using three primary colors. This enables a dynamic display of the relationships among multiple genes (e.g., Ahox1, AMD1, As-T, etc. In Figs. 1 & 34), which was impossible by merely displaying a change in a single gene in terms of embryogenesis in chronological order. Thus, the sequence of events wherein an increase of expression of a certain gene brings about an increase or decrease of expression of another gene, which affects other factors, and so on, can be visualized. This effective method also supports the effects of claims 3 and 5.

None of the cited prior art references teach or suggest such a feature.

Applicants contend that neither the cited references, nor their combination teaches or discloses each and every feature of the present invention as disclosed in independent claims 3, 5-7, 14-15 and 23. As such, the present invention as now claimed is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

Conclusion

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art references upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of

the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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